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Original Article

The Efficacy of Intratympanic Steroid Injection in Tinnitus Cases Unresponsive to Medical Treatment

Haydar Murat Yener, Elif Sarı, Mehmet Aslan, Umur Yollu, Emine Deniz Gözen, Ender İnci

Department of Otorhinolaryngology, İstanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, İstanbul, Turkey

ORCID iDs of the authors: H.M.Y. 0000-0002-0932-2773; E.S. 0000-0003-4618-6341; M.A. 0000-0002-0707-9984; U.Y. 0000-0002-2975-8902; E.D.G. 0000-0002-2586-3721; E.İ. 0000-0002-5607-8734.

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OBJECTIVES: To examine the efficacy of an intratympanic steroid injection in tinnitus cases unresponsive to medical treatment.

MATERIALS and METHODS: The study was carried out at the Ear, Nose, and Throat Department with 107 patients (46 male, 61 female) between the ages of 20 and 77 with a mean of 42.8 years who had idiopathic tinnitus. Patients were randomized by simple randomization to receive intratympanic dexamethasone or isotonic solution. The patients received six intratympanic injections, two per week for three weeks. Tinnitus handicap index (THI) was performed before treatment and at first week, first month, and six months after the completion of the study protocol. The audiometric tests were performed six months after the treatment.

RESULT: In the study group, pretreatment THI and post-treatment first month THI scores and pretreatment THI and post-treatment sixth month THI scores were significantly different whereas the same scores were not significantly different in the control group. The comparison of THI scores between the groups revealed significantly lower scores in the first and sixth months for the study group.

CONCLUSION: The effect of the intratympanic injection of dexamethasone on the efficacy of treatment of tinnitus severity was statistically significant.

KEYWORDS: Intratympanic injection, inventory, tinnitus, treatment

INTRODUCTION

Tinnitus is a disabling symptom that can occur alone or with other disorders such as hearing loss [1] and can be defined as the perception of sound without an external stimulus [2]. Subjective tinnitus is the most common form of tinnitus and can be detected in nearly 10% of the general population [3]. The most common site for subjective tinnitus is the cochlea but other disorders within the auditory pathway may also be responsible [3]. Among cochlear pathologies, the most common diagnoses include presbyacusis followed by noise-induced hearing loss and endolymphatic hydrops [4]. The prevalence of subjective tinnitus increases typically with aging and it is clearly associated with hearing loss [5]. Other factors associated with tinnitus are noise exposure, head injuries, middle ear disorders, ototoxic drugs, and Meniere's disease but idiopathic cases are the most prevalent group [6].

Patients with tinnitus should be evaluated comprehensively and the underlying factors should be determined. Several different options have been described for tinnitus treatment, which include tinnitus retraining, tinnitus masking, biofeedback therapy, various drug treatments, and more recently, intratympanic injection therapy [2, 3, 6]. The most frequently used drugs for intratympanic injections are aminoglycoside antibiotics and steroids. Steroids, which have anti-inflammatory and electrolyte modifying effects, are one of the most popular agents used for intratympanic treatment [6]. Intratympanic dexamethasone treatment has been demonstrated as relatively safe compared to gentamicin and lidocaine [7, 8]. Corticosteroids are frequently used to treat inner ear disorders such as autoimmune inner ear disease, sudden hearing loss, and Meniere's disease [9, 10].

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Corresponding Address: Haydar Murat Yener E-mail: hmuratyener@gmail.com

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The therapeutic effect of intratympanic drugs is thought to occur by diffusion through round window, annular ligament of oval window, capillaries, or through the lymphatics of the inner ear. However, the effectiveness of the intratympanic therapy for tinnitus has not yet been proven [6, 11, 12]. There have been conflicting results pertaining to the effects of intratympanic steroids on tinnitus. Araujo and colleagues did not find any benefit in the intratympanic injection of dexamethasone over the isotonic injection in the treatment of severe tinnitus [12]. However Sakata et al. [13] reported the total resolution of tinnitus in 63% of the cases treated with intratympanic steroids. Due to the inconsistency of results and the lack of convincing proof for the effects of intratympanic steroids on tinnitus, we conducted a prospective study on patients with subjective tinnitus who were treated either with intratympanic dexamethasone or saline injections and evaluated these patients with audiometric tests and the Tinnitus Handicap Inventory (THI).

MATERIALS AND METHODS

The study was carried out at the Ear, Nose, and Throat Department following the approval of the study protocol by the İstanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine Ethics Committee. The patients with tinnitus for more than six months were enrolled, with each patient providing informed written consent.

After a detailed evaluation of the nature and duration of the tinnitus and past medical history, a complete otorhinolaryngology examination was performed in all patients. Also otomicroscopy and audiometric examinations, including pure tone audiometry, impedencemetry, otoacoustic emissions, and auditory brainstem response tests were carried out.

The patients were also screened by blood cell count, serum electrolytes, glucose, cholesterol, and triglyceride levels and thyroid function tests. Patients with otitis media, endolymphatic hydrops or otosclerosis, and systemic diseases like hypertension, hypercholesterolemia, thyroid abnormalities, and diabetes mellitus were excluded. A total of 107 patients (46 male, 61 female) between the ages of 20 and 77 with a mean age of 42.8 years who had idiopathic tinnitus were included in this prospective study. Patients were randomized by simple randomization to receive intratympanic dexamethasone or the same amount of isotonic solution. The injections were administered twice a week for three weeks. The study group (IT steroid) composed of 60 patients [26 male, 34 female; ages ranging between 21 and 77 with a mean of 42.43 (±14.3) years] and the control group (IT saline) composed of 47 patients [20 male, 27 female; ages ranging between 20 and 67 with a mean of 43.28 (±13.3) years]. The patients were evaluated using the Turkish version of THI.

MAIN POINTS

- Tinnitus is a disabling symptom that can occur alone or with other disorders.
- Corticosteroids are frequently used to treat inner ear disorders.
- Current treatment of tinnitus have limited efficacy.
- Intratympanic dexamethasone is an effective method in the treatment of subjective tinnitus.

THI is a highly reliable test, which is not affected by age, gender, or hearing loss. The test gives clear measurements and can be applied easily. There are three options for each question in the THI: "yes," "no," and "sometimes" with points 4, 0, and 2, respectively.

THI was performed before treatment and at first week, first month, and six months after the completion of the study protocol. The audiometric tests were performed before treatment and six months after treatment. Patients were administered 0.5-mL intratympanic injections of either 4 mg/mL dexamethasone or isotonic solution. Following xylocaine spray application to achieve topical anesthesia, the patients were placed supine with their heads turned about 45° to the opposite side. Using a 25-gauge needle, the assigned solution was injected through the postero-inferior quadrant of the tympanic membrane, and the patients stayed in the same position for about 10 minutes. A total of six injections were performed and pre-treatment and post-treatment THI scores and audiologic test results were compared.

Statistical Analysis

The mean, standard deviation, and rate were used for descriptive analysis. Chi-squared test and Student's t test were used for intergroup evaluations, and paired-t test was used for intragroup evaluations. The Statistical Packaged for the Social Sciences (SPSS) version 22.0 software (IBM Corp.; Armonk, NY, USA) was used for statistical analysis. The results were evaluated at the level of significance $p<0.05$.

RESULTS

The demographic data and statistical results of the 107 patients are presented in Tables 1 and 2. The study group (IT steroid) comprised of 60 patients [26 male, 34 female; ages ranging between 21 and 77 with a mean of 42.43 (±14.3) years] and the control group (IT saline) comprised of 47 patients [20 male, 27 female; ages ranging between 20 and 67 with a mean of 43.28 (±13.3) years]. No age differences were revealed between the two groups ($p>0.05$) (Table 1).

Forty patients in the study group and 33 patients in the control group were non-smokers, and there was no statistical difference among the groups. OAE was present in 34 patients in the study group and in 17 patients in the control group without any significant difference (Table 1).

In the study group, 18 patients had tinnitus on the right, 24 had tinnitus on the left, and 18 had bilateral tinnitus. In the control group, tinnitus was right sided in 12, left sided in 14, and bilateral in 21 patients.

The duration of tinnitus in the study group ranged from 12 to 120 months with a mean duration of 35.28±22.67 months. Patients in the control group had tinnitus for a mean of 36.87±21.38 months (range 12-96 months). No differences in duration were revealed between the two groups ($p>0.05$) (Table 1).

The mean pure-tone average on the left side in the study group was 26.27±27.76 dB HL before treatment and 27.43±29.88 dB HL after treatment. The mean pure-tone average on the right side in study group was 23.70±19.06 dB HL before treatment and 22.70±18.11 dB HL after treatment. There were no differences in the pre-treatment and post-treatment mean pure-tone averages on the left and right sides in the study group (Table 2).

Table 1. Demographics, pre-treatment, and post-treatment THI scores, pre-treatment and post-treatment pure tone averages of the study and control groups

	Range	Mean±Std Dev	Range	Mean±Std Dev	p
Age	21-77	42.43±14.32	20-67	43.28±13.3	0.754
Gender (F/M)	34/26		27/20		0.201
Duration	12-120	35.28±22.67	12-96	36.87±21.38	0.711
Smoking (-/+)	40/20		33/14		0.365
OAE (-/+)	26/34		30/17		0.395
pretx THI	10-98	57.33±24.94	12-98	57.96±24.39	0.897
post tx 1 wk THI	10-100	52±27	16-94	58.04±22.73	0.212
post tx 1 mo THI	10-100	48.93±27.62	14-94	58.68±23.25	0.050
post tx 6 mo THI	10-100	46.13±28.79	14-86	56.77±23.13	0.037
pretx pure tone average-right	5-60	23.7±19.06	6-93	26.08±21.65	0.606
pretx pure tone average-left	5-120	26.27±27.76	10-45	21.63±11.59	0.313
posttx pure tone average-right	5-66	22.7±18.11	8-88	27.23±20.73	0.305
postx pure tone average-left	5-120	27.43±29.88	8-60	23.59±15.59	0.464

Table 2. Statistical analysis of pretreatment and posttreatment Tinnitus Handicap Index scores in study and control groups at 1st week, 1st month, 6th month and pretreatment and posttreatment pure tone averages. Significant values marked bold.

	Study Group	Control Group
	p	p
pretx THI&post tx 1 wk THI	0.08	0.954
pretx THI&post tx 1 mo THI	0	0.655
pretx THI&post tx 6 mo THI	0	0.468
pretx and pos tx pure tone average-right	0.718	0.054
pretx and pos tx pure tone average-left	0.476	0.157

Pre-treatment and post-treatment mean pure-tone average scores of the control group on the left side were 21.63±11.59 dB and 23.59±15.59 dB respectively. Mean pre-treatment and post-treatment pure-tone scores on the right side were 26.08±21.65 and 27.23±20.73 respectively. There were no differences in the pre-treatment and post-treatment mean pure-tone averages on the left and right sides in the control group (Table 2).

The mean pre-treatment and post-treatment at first week, post-treatment at first month, and post-treatment at sixth month THI scores of the study group were 57.33±24.9, 52±27, 48.93±27.62, and 46.13±28.79 respectively. The mean pre-treatment and post-treatment at first month and pre-treatment and post-treatment at sixth month THI scores of the control group were 57.96±24.39, 58.04±22.73, 58.68±23.25, and 56.77±23.13 respectively. In the study group, pretreatment and post-treatment THI scores at the first month and pre-treatment and post-treatment THI scores at six months were significantly different (Table 2) whereas the same scores were not significantly different in the control group (Table 2). The comparison of the THI scores between the groups revealed significantly lower scores at the first and sixth months in the study group (p=0.05 and 0.037 respectively) (Table 1).

There were no complications like increased hearing thresholds, increased perception of tinnitus, vertigo, and tympanic membrane perforation during the course of the therapy and the follow-up period.

DISCUSSION

Treatment of tinnitus currently includes hearing aids with masking, tinnitus retraining therapy, and oral medications which have limited efficacy. Intratympanic treatment with various agents is an emerging treatment option for inner ear disorders currently. This treatment has been used in sudden sensorineural hearing loss, Meniere's disease, tinnitus associated with these disorders, and idiopathic tinnitus [6, 11, 12, 14, 15].

Intratympanic steroids diffuse through the round window and show their anti-inflammatory and electrolyte modifying effects by the steroid receptors which have been demonstrated in animals and humans [16, 17]. The underlying mechanism of steroids in tinnitus is to reduce the inflammation caused by immunomediated/autoimmune dysfunction or a direct effect on the inner ear epithelium [7]. Increased cochlear blood flow has also been suggested as another mechanism [18, 19]. The advantages of intratympanic steroid injections are the avoidance of systemic side effects providing high concentrations to the inner ear. In our study, we administered intratympanic dexamethasone injections to patients with refractory chronic tinnitus to other medications. By inducing high concentrations of the steroid in the inner ear without systemic side effects, we observed that steroids could reduce tinnitus perception significantly without a significant effect on hearing levels. This effect may mainly be attributable to increased blood flow in the inner ear.

The most important factors that determine the efficacy of the intratympanic treatment of tinnitus is time and drug dose. Intratympanic perfusion time and frequency is one of the key factors determining the effectiveness of treatment [20]. Shim et al. [21] stated that the intratympanic steroid injection (ITSI) was effective in treating newly developed tinnitus. The efficacy of treatment decreases with prolonged tinnitus [12]. Sakata et al. [13] treated 1,214 tinnitus patients with intratympanic dexamethasone injections (ITDI). They found that 77% of the patients'

symptoms decreased immediately and 68% after six months [12]. In 2000, Shulman and Goldstein treated 10 patients with ITDI and reported that tinnitus was improved in about 70% of their subjects [22]. In 2002, Cesarani et al. [11] following intratympanic steroids for tinnitus treatment reported complete resolution in 34% of the patients, significant improvement in 40%, and no change in 26%. Most of the papers about this subject state that intratympanic steroid injections are mostly effective in patients with acute tinnitus and mostly demonstrate no effect in those with chronic tinnitus. A recent study by Choi et al. [23] found no effect following intratympanic steroid injections after four weeks. Previous studies also could not demonstrate the effect of steroids over placebo. Topak et al. [24], following a three-week intratympanic steroid injection routine, evaluated patients after two weeks and did not detect a significant difference between the steroid and the placebo. However, in our patient group, we found a significant reduction in tinnitus at the fourth week and the sixth month. In contrast to our study, in the aforementioned studies, the patients were evaluated at second and fourth weeks. Our follow-up period was longer, and at fourth and sixth months, a significant reduction was detected, which might be due to the late effect of the intratympanic treatment. Another mechanism at work may be the steroid-induced increase in the blood flow to the inner ear. Additionally, the injection protocols and drugs and drug concentrations in the previous studies and in our study were not standard. This could be another reason for the conflicting results.

The results of this study show that intratympanic dexamethasone was effective in the treatment of subjective tinnitus. Intratympanic treatment was demonstrated to improve tinnitus scores in the study group.

CONCLUSION

The treatment efficacy of the intratympanic injection of dexamethasone on tinnitus severity was statistically significant ($p<0.05$). The patients experienced no complications or side effects, and we believe that intratympanic steroid injections could be considered as a viable option for the treatment of tinnitus.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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